10088200 .072202 15 MAR 2002

JC05 Rec'd PCT/PTO

FORM PTO-1390 (REV 5-93) U S DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NUMBER: **127FR/50898**

U S APPLICATION NO (if known, see 37 CFR): ~~Not Yet Assigned~~ 10/088200

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/DE00/02609	**3 August 2000**	**15 September 1999**

TITLE OF INVENTION
MICROSENSOR FOR MEASURING THE POSITION OF LIQUIDS IN CAPILLARIES

APPLICANT(S) FOR DO/EO/US
Thomas LISEC, Bernd WAGNER and Hans Joachim QUENZER

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1.	X	This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.		
2.		This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371		
3.		This express request to begin national examination procedures (35 U.S.C. 371(f) at any time rather than delay Examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).		
4.	X	A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.		
5.	X	A copy of the International Application as filed (35 U.S.C. 371(c)(2)).		
		a.		is transmitted herewith (required only if not transmitted by the International Bureau).
		b.	X	has been transmitted by the International Bureau
		c.		is not required, as the application was filed in the United States Receiving Office (RO/US)
6.	X	A translation of the International Application into English (35 U.S.C. 371(c)(2)).		
7.		Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))		
		a.		are transmitted herewith (required only if not transmitted by the International Bureau).
		b.		have been transmitted by the International Bureau.
		c.		have not been made; however, the time limit for making such amendments has NOT expired.
		d.		have not been made and will not be made.
8.		A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).		
9.	X	An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)) **(UNEXECUTED)**		
10.	X	A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).		

Item 11. to 16. below concern other document(s) or information included:

11.	X	An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12.		An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13.	X	A FIRST preliminary amendment.
		A SECOND or SUBSEQUENT preliminary amendment.
14.	X	A substitute specification and marked-up copy thereof.
15.		A change of power of attorney and/or address letter.
16.	X	Other items or information:

a. PCT/IPEA/416 and 409 International Preliminary Examination Report with (1) amended sheet
b. PCT/IB308; PCT/IB/301; and PCT/IB/332
c.

JC13 Rec'd PCT/PTO 15 MAR 2002

U.S. APPLICATION NO (if known, see 37 CFR 1 5	INTERNATIONAL APPLICATION NO	ATTORNEY'S DOCKET NUMBER
Not Yet Assigned 10/088200	PCT/DE00/02609	127FR/50898

17. [X] The following fees are submitted:				CALCULATIONS	PTO USE ONLY
Basic National Fee (37 CFR 1.492(a)(1)-(5)): Search Report has been prepared by the EPO or JPO $ 890.00				$ 890.00	
International preliminary examination fee paid to USPTO (37 CFR 1.482) $ 690.00					
No international preliminary examination fee paid to USPTO (37 CFR 1.482) but international search fee paid to USPTO (37 CFR 1.445(a)(2) $ 740.00					
Neither international preliminary examination fee (37 CFR 1.482) nor International search fee (37CFR 1.445(a)(2) paid to USPTO $ 1000.00					
International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(2)-(4) $ 100.00					
ENTER APPROPRIATE BASIC FEE AMOUNT =				$ 890.00	
Surcharge of $130.00 for furnishing the oath or declaration later than [ ] 20 [ ] 30 months from the earliest claimed priority date (37 CFR 1.492(e)).				$ 0.00	
Claims	Number Filed	Number Extra	Rate		
Total Claims	20 - 20 =	0	X $18.00	$0.00	
Independent Claims	5- 3 =	2	X $84.00	$168.00	
Multiple dependent claims(s) (if applicable)			+ $280.00	$0.00	
TOTAL OF ABOVE CALCULATIONS=				$ 1058.00	
Applicant claims Small Entity Status (See 37 CFR §1.27) [ ] yes [ ] no. Reduction by 1/2 for filing by small entity, if applicable.				$0.00	
SUBTOTAL =				$1058.00	
Processing fee of $130.00 for furnishing the English translation later than [ ] 20 [ ] 30 months from the earliest claimed priority date (37 CFR 1.492(f)).				$ 0.00	
TOTAL NATIONAL FEE =				$1058.00	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28,3.31). $40.00 per property +				$	
TOTAL FEE ENCLOSED =				$1058.00	
				Amount to be: refunded	$
				Charged	$

a. [X] A check in the amount of $1058.00 for the filing fee.

b. [ ] Please charge my Deposit Account No. ______ in the amount of $______ to cover the above fees. A duplicate copy of this sheet is enclosed.

c. [X] The Commissioner is hereby authorized to charge any additional fees, which may be required, or credit any overpayment to Deposit Account No. 05-1323 . A duplicate copy of this sheet is enclosed.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:	
Crowell & Moring, LLP	SIGNATURE
P.O. Box 14300	Vincent J. Sunderdick
Washington, D.C. 20044-4300	NAME: Vincent J. Sunderdick
Tel. No. (202) 624-2500	
Fax No. (202) 628-8844	REGISTRATION NUMBER: 29,004
	DATE : March 15, 2002

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Attorney Docket: 127FR/50898
PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: THOMAS LISEC ET AL

Serial No.: Not Yet Assigned

Filed: Concurrently Herewith

Title: MICROSENSOR FOR MEASURING THE POSITION OF LIQUIDS IN CAPILLARIES

PRELIMINARY AMENDMENT

Box PCT
Commissioner for Patents
Washington, D.C. 20231

Sir:

Please enter the following amendments to the specification and claims (noting that claim 1 was amended by way of Annexes to the International Preliminary Examination Report for PCT/DE00/02609), prior to the examination of the application during the U.S. National Phase.

IN THE SPECIFICATION:

A substitute specification and a marked-up copy thereof is attached herewith.

IN THE CLAIMS:

Please amend claims 1-17 as follows:

(A copy of the marked-up version of amended claims 1-17 are attached to this Preliminary Amendment).

1. (Amended) A sensor element for electrically measuring the position of liquid levels, comprising:

a substrate; and

a plurality of electrodes adapted to be contacted individually and mounted on the substrate, wherein the electrodes comprise sensor-active partial electrodes that are networked with electrical connections, and wherein the partial electrodes of two respective electrodes are always positioned opposite one another, separated by a distance, to form partial electrode pairs, and the electrode pairs thus formed recur periodically over a length of the sensor element.

2. The sensor element according to Claim 1, wherein the electrical connections of the networked partial electrodes are coated with a passivating layer.

3. The sensor element according to Claim 1, wherein the partial electrodes positioned pairwise opposite one another are always at least one of separated by the same distance, and the distances between the partial electrode pairs in the longitudinal direction of the sensor element are constant over the entire length of the sensor element, and/or the number of partial electrode pairs per electrode pair is constant.

4. The sensor element according to Claim 1, wherein the distance between the partial electrode pairs in the longitudinal direction is approxiamatley100 μm.

5. The sensor element according to Claim 1, wherein the substrate is made of one of silicon, glass, and plastic.

6. The sensor element according to Claim 1, wherein the electrodes are made of one of platinum, iridium, and gold.

7. The element according to Claim 1, wherein the sensor chip surface has wetting properties such that the boundaries of the liquid wetting of the sensor surface correspond to the liquid level.

8. An arrangement for measuring a capillary filling, including a sensor element for electrically measuring the position of liquid levels, comprising

a substrate; and

a plurality of electrodes adapted to be contacted individually and mounted on the substrate,

wherein the electrodes comprise sensor-active partial electrodes that are networked with electrical connections, and wherein the partial electrodes of two respective electrodes are always positioned opposite one another, separated by a distance, to form partial electrode pairs, and the electrode pairs thus formed recur periodically over a length of the sensor element, wherein the sensor element is attached to a capillary in such a way that the sensor-active partial electrodes are situated inside the capillary and the electrical connection options are situated outside the capillary, and that at least one conductivity boundary of the capillary filling is located in the region of the sensor element.

9. The arrangement according to Claim 8, wherein two conductivity boundaries of operating liquids in the capillary form a bubble in the region of the sensor element, said bubble being bounded on both sides by the operating liquid.

10. The arrangement according to Claim 8, wherein at least one of the bubble is filled with gas, and the length of the bubble is approximately twice the

length of an electrode pair in the longitudinal direction, and the same operating liquid is present on both sides of the bubble.

11. A method for measuring liquid levels using a sensor element for electrically measuring the position of liquid levels, comprising

a substrate; and

a plurality of electrodes adopted to be contacted individually and that are mounted on the substrate, wherein the electrodes comprise sensor-active partial electrodes that are networked with electrical connections, wherein the partial electrodes of two respective electrodes are always positioned opposite one another, separated by a distance, to form partial electrode pairs,

and the electrode pairs thus formed recur periodically over a length of the sensor element comprising the steps of:

determining which electrode pairs are covered and which are not covered by an operating liquid by measuring the resistance of each individual electrode pair in an idle state of the operating liquid;

comparing the resistance values to characteristic minimum and maximum values for liquid coverage or no liquid coverage; and

detecting from this information the position of the conductivity boundary or of the bubble on a specific electrode pair.

12. A method for measuring liquid levels using a sensor element for electrically measuring the position of liquid levels, comprising

a substrate; and

a plurality of electrodes adapted to be contacted individually and mounted on the substrate,

wherein the electrodes comprise sensor-active partial electrodes that are networked with electrical connections, and wherein the partial electrodes of two respective electrodes are always positioned opposite one another, separated by a distance, to form partial electrode pairs,

and the electrode pairs thus formed recur periodically over a length of the sensor element comprising the steps of:

comparing the intermediate value lying between the minimum and maximum resistance value of the electrode pair to a reference resistance curve of the electrode pair; and

obtaining the position of the conductivity boundary for a specific partial electrode pair from said step of comparing.

13. The method according to Claim 11, wherein the path distance traveled by the bubble is determined from the detected position of the bubble or of the conductivity boundary before and after movement of the bubble.

14. A method for measuring liquid levels using a sensor element for electrically measuring the position of liquid levels, comprising

a substrate; and

a plurality of electrodes adapted to be contacted individually and mounted on the substrate, wherein the electrodes comprise sensor-active partial electrodes that are networked with electrical connections, and wherein the partial electrodes of two respective electrodes are always positioned opposite one another, separated by a distance, to form partial electrode pairs, and the electrode pairs thus formed recur periodically over a length of the sensor element comprising the steps of:

jumps in the resistance values upon movement of a bubble by parallel monitoring of the resistance values of all electrode pairs; and

determining the path distance traveled by the bubble from the number of jumps.

15. The method according to Claim 13, wherein the displaced liquid volume is determined from the path distance traveled.

16. The method according to Claim 11, wherein the resistance measurement of the electrode pairs is performed by measuring the resulting current after an alternating current is applied to the electrodes.

17. The method according to Claim 16, wherein the alternating current has a frequency in the kilohertz range and/or an amplitude in the range of 100 millivolts.

Please add the following new claims:

--18. The method according to Claim 14, wherein the displaced liquid volume is determined from the path distance traveled.

19. The method according to Claim 12, wherein the resistance measurement of the electrode pairs is performed by measuring the resulting current after an alternating current is applied to the electrodes.

20. The method according to Claim 13, wherein the resistance measurement of the electrode pairs is performed by measuring the resulting current after an alternating current is applied to the electrodes.--

IN THE ABSTRACT:

Please substitute the new Abstract of the Disclosure submitted herewith on a separate page for the original Abstract presently in the application.

REMARKS

Entry of the amendments to the specification and claims, (noting that claim 1 was amended by way of Annexes to the International Preliminary Examination Report for PCT/DE00/02609), before examination of the application in the U.S. National Phase is respectfully requested. If there are any questions regarding this Preliminary Amendment or this application in general, a telephone call to the undersigned would be appreciated since this should expedite the prosecution of the application for all concerned.

If necessary to effect a timely response, this paper should be considered as a petition for an Extension of Time sufficient to effect a timely response, and please charge any deficiency in fees or credit any overpayments to Deposit Account No. 05-1323 (Docket #127FR/50898).

Respectfully submitted,

Date: March 15, 2002

Vincent J. Sunderdick

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VJS/leb

ABSTRACT OF THE DISCLOSURE

A sensor element for electrically measuring the position of liquid levels, comprising a substrate (2) and a plurality of electrodes (3) that can be contacted individually and that are mounted on the substrate, characterized in that the electrodes comprise sensor-active partial electrodes (5) that are networked with electrical connections (7), with the partial electrodes of two respective electrodes always being positioned opposite one another, separated by a distance, as partial electrode pairs (11), and with the electrode pairs (8) thus formed recurring periodically over the length of the sensor. Quasi-digital measuring methods are derived from the behavior of the impedance of the electrode pairs, whereby the liquid level is measured by detecting a conductivity boundary in a capillary filling.

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Please amend claims 1-17 as follows:

1. (Amended) [Sensor] A sensor element for electrically measuring the position of liquid levels, [having] comprising:

a substrate [(2)]; and

a plurality of electrodes [(3) that can be] adapted to be contacted individually and [that are] mounted on the substrate, [whereby] wherein the electrodes comprise sensor-active partial electrodes [(5)] that are networked with electrical connections [(7)], and wherein [whereby] the partial electrodes of two respective electrodes are always positioned opposite one another, separated by a distance, [as] to form partial electrode pairs [(11)], and the electrode pairs [(8)] thus formed recur periodically over [the] a length of the sensor element.

2. [Sensor] The sensor element according to Claim 1, [characterized in that] wherein the electrical connections [(7)] of the networked partial electrodes are coated with a passivating layer [(6)].

3. [Sensor] The sensor element according to [one of Claims 1 or 2, characterized in that] Claim 1, wherein the partial electrodes positioned pairwise opposite one another are always at least one of separated by the same distance, and[/or] the distances between the partial electrode pairs in the longitudinal direction of the sensor element are constant over the entire length of the sensor element, and/or the number of partial electrode pairs per electrode pair is constant.

4. [Sensor] The sensor element according to [at least one of Claims 1 through 3, characterized in that] Claim 1, wherein the distance between the

partial electrode pairs in the longitudinal direction is [in the range of] approxiamatley100 μm.

5. [Sensor] The sensor element according to [at least one of Claims 1 through 4, characterized in that] Claim 1, wherein the substrate is made of one of silicon, glass, [or] and plastic.

6. [Sensor] The sensor element according to [at least one of Claims 1 through 5, characterized in that] Claim 1, wherein the electrodes are made of one of platinum, iridium, [or] and gold.

7. [Sensor] The element according to [at least one of Claims 1 through 6, characterized in that] Claim 1, wherein the sensor chip surface has wetting properties such that the boundaries of the liquid wetting of the sensor surface correspond to the liquid level.

8. [Arrangement in which the sensor element according to at least one of Claims 1 through 7 is used] An arrangement for measuring a capillary filling, [characterized in that] including a sensor element for electrically measuring the position of liquid levels, comprising

a substrate; and

a plurality of electrodes adapted to be contacted individually and mounted on the substrate,

wherein the electrodes comprise sensor-active partial electrodes that are networked with electrical connections, and wherein the partial electrodes of two respective electrodes are always positioned opposite one another, separated by a distance, to form partial electrode pairs, and the electrode pairs thus formed recur periodically over a length of the sensor element, wherein the sensor element is attached to a capillary in such a way that the sensor-active partial

electrodes [(5)] are situated inside the capillary and the electrical connection options are situated outside the capillary, and that at least one conductivity boundary of the capillary filling is located in the region of the sensor element.

9. [Arrangement in which the sensor element is used according to at least one of Claims 1 through 7 and] The arrangement according to Claim 8, [characterized in that] wherein two conductivity boundaries of operating liquids in the capillary form a bubble in the region of the sensor element, said bubble being bounded on both sides by the operating liquid.

10. [Arrangement in which the sensor element is used according to at least one of Claims 1 through 7 and Claims 8 or 9, characterized in that] The arrangement according to Claim 8, wherein at least one of the bubble is filled with gas, and[/or] the length of the bubble is approximately twice the length of an electrode pair in the longitudinal direction, and[/or] the same operating liquid is present on both sides of the bubble.

11. [Method] A method for measuring liquid levels using [the arrangement according to at least one of Claims 1 through 8 and 9 and/or 10, characterized in that it is determined which] a sensor element for electrically measuring the position of liquid levels, comprising

a substrate; and

a plurality of electrodes adopted to be contacted individually and that are mounted on the substrate, wherein the electrodes comprise sensor-active partial electrodes that are networked with electrical connections, wherein the partial electrodes of two respective electrodes are always positioned opposite one another, separated by a distance, to form partial electrode pairs,

and the electrode pairs thus formed recur periodically over a length of the sensor element comprising the steps of:

determining which electrode pairs are covered and which are not covered by [the] an operating liquid by measuring the resistance of each individual electrode pair in [the] an idle state of the operating liquid; [and]

comparing the resistance values to [the] characteristic minimum and maximum values for liquid coverage or no liquid coverage[,]; and

detecting from this information the position of the conductivity boundary or of the bubble on a specific electrode pair [is detected].

12. [Method] A method for measuring liquid levels using [the arrangement according to at least one of Claims 1 through 8 and 9 and/or 10, characterized in that the position of a conductivity boundary within an electrode pair in the idle state of the operating liquid is determined by] a sensor element for electrically measuring the position of liquid levels, comprising

a substrate; and

a plurality of electrodes adapted to be contacted individually and mounted on the substrate,

wherein the electrodes comprise sensor-active partial electrodes that are networked with electrical connections, and wherein the partial electrodes of two respective electrodes are always positioned opposite one another, separated by a distance, to form partial electrode pairs,

and the electrode pairs thus formed recur periodically over a length of the sensor element comprising the steps of:

comparing the intermediate value lying between the minimum and maximum resistance value of the electrode pair to a reference resistance curve of the electrode pair[,]; and

obtaining the position of the conductivity boundary for a specific partial electrode pair from said step of comparing [is thereby obtained].

13. [Method] The method according to [at least one of Claims 11 or 12, characterized in that] Claim 11, wherein the path distance traveled by the bubble is determined from the detected position of the bubble or of the conductivity boundary before and after movement of the bubble.

/114. [Method] A method for measuring liquid levels using [the arrangement according to at least one of Claims 1 through 8 and 9 and/or 10, characterized in that] a sensor element for electrically measuring the position of liquid levels, comprising

a substrate; and

a plurality of electrodes adapted to be contacted individually and mounted on the substrate, wherein the electrodes comprise sensor-active partial electrodes that are networked with electrical connections, and wherein the partial electrodes of two respective electrodes are always positioned opposite one another, separated by a distance, to form partial electrode pairs, and the electrode pairs thus formed recur periodically over a length of the sensor element comprising the steps of:

jumps in the resistance values upon movement of a bubble [are detected] by parallel monitoring of the resistance values of all electrode pairs[,]; and

determining the path distance traveled by the bubble [is determined] from the number of jumps.

15. [Method] The method according to [at least one of Claims 13 or 14, characterized in that] Claim 13, wherein the displaced liquid volume is determined from the path distance traveled.

16. [Method] The method according to [at least one of Claims 11 through 15, characterized in that] Claim 11, wherein the resistance measurement of the electrode pairs is performed by measuring the resulting current after an alternating current is applied to the electrodes.

17. [Method] The method according to Claim 16, [characterized in that] wherein the alternating current has a frequency in the kilohertz range and/or an amplitude in the range of 100 millivolts.

10088200 10/088200

JC13 Rec'd PCT/PTO 15 MAR 2002

Attorney Docket: 127FR/50898
PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: THOMAS LISEC ET AL

Serial No.: Not Yet Assigned

Filed: Concurrently Herewith

Title: MICROSENSOR FOR MEASURING THE POSITION OF LIQUIDS IN CAPILLARIES

SUBMISSION OF SUBSTITUTE SPECIFICATION

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Attached is a Substitute Specification and a marked-up copy of the original specification. I certify that said substitute specification contains no new matter and includes the changes indicated in the marked-up copy of the original specification.

Respectfully submitted,

Date: March 15, 2002

Vincent J. Sunderdick

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SUBSTITUTE SPECIFICATION

TITLE OF THE INVENTION

Microsensor for Measuring the Position of Liquids in Capillaries

BACKGROUND AND SUMMARY OF THE INVENTION

[0001] This application claims the priority of German Application No. 199 44 331.5, filed, September 15, 1999 and International Application No. PCT/DE00/02609, filed August 3, 2000, the disclosures of which are expressly incorporated by reference herein.

[0002] The invention relates to a microsensor for measuring the position of liquids in capillaries which is particularly well suited for use in automated pipetting dispensers in medical laboratories and in the pharmaceutical industry.

[0003] In the analysis of clinical profiles or routine health checks, modern medicine increasingly relies on the quantitative determination of relevant substances in bodily fluids. The number of substances to be monitored is constantly growing, as is likewise the frequency of testing. Performing greater numbers of analyses while simultaneously lowering costs primarily requires a decrease in the use of reagents, which are often very costly. The tendency toward precise metering of the smallest possible quantities of liquids, with a volumetric range of 0.1 to 20 μL, is therefore a key objective.

[0004] In the metering operation, defined quantities of samples and reagents from starting containers must be distributed onto microtiter plates having many individual reaction receptacles (wells). A conventional plastic microtiter plate contains 96 wells, for example, each with a volume of 500 μL, in a 9-mm grid. Modern pipetting systems can meter between one and several hundred μL of a liquid, using stepping

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motor-driven injection pumps, with a piston injection precision of several percent. Typically, eight separately controllable pipettes are arranged in parallel, with the result that a microtiter plate must be filled in several passes. The throughput is therefore limited, which affects the measuring results in kinetic tests. Devices currently exist which contain 96 pipettes. However, such devices are not separately controllable; that is, with each metering operation the same quantity is dispensed to all the pipettes. In many applications, separate control of the pipettes would be preferable. In order to meter quantities of liquids from 0.1 to 20 µL with greater precision in an array of separately controllable pipettes, the metering operation must be actively monitored at each individual pipette.

[0005] In the course of a quantitative analysis, samples and reagents are successively pipetted into the appropriate wells of the microtiter plate, using an injection pump via a liquid column. The operating liquid is typically separated from the sample or reagent by an air bubble to avoid contamination. After the reactions have taken place in the wells, the concentration of one of the reaction products is photometrically determined, and the concentration of the sample component being sought is calculated therefrom.

[0006] The sample volume dispensed during a pipetting operation results from the piston feed from the injection pump. However, the sample volume is defined in the same manner both before and after the metering operation by the filling level of the sample liquid in the pipette.

[0007] Filling level sensors for monitoring liquids in reservoirs or tanks have been known for quite some time. In addition to sensors that are based on floats, there are

a number of systems with no moving parts. Such systems are based, for example, on optical or electrical measurement techniques.

[0008] U.S. Patent 5,138,880 describes a capacitive sensor comprising two concentric cylinders which are submerged in a dielectric medium along the measurement axis. The cylinders are divided into a number of discrete condensers. The capacitance of each individual condenser depends on whether air or the medium to be monitored is present between the electrodes. By comparison of the capacitances, the filling height of the medium in the container may be quasi-digitally determined with a precision corresponding to the number of measurement segments. The capacitive measurement principle can also be employed in the form of a planar sensor. This type of sensor must be calibrated for each liquid.

[0009] The filling level may be potentiometrically determined in conductive liquids. A rod-shaped resistor, which is vertically submerged in the liquid and together with this liquid forms the resistors of a bridge circuit, may serve as the measuring probe. The voltage drop at the resistor, measured via the liquid, is proportional to the liquid level. An example of such is disclosed in U.S. Patent 5,146,785. Here, the measuring probe is additionally divided into a series of individual resistors, thus generating a stair-step, quasi-digital output signal.

[0010] A further electrical sensor principle is based on conductivity measurements. To this end, an alternating current in the kHz range is applied between two respective electrodes, and the current between the electrode pairs is measured. An example of such is disclosed in U.S. Patent 5,719,556.

SUBSTITUTE SPECIFICATION

[0011] The electrical devices for measuring liquid levels according to the current art are not suited for measuring the position of liquids in capillaries. The use of said devices is limited to the measurement of filling levels in tanks, for example.

[0012] The object of the invention is to provide a device and a method for operating said device for electrically measuring the position of liquid levels in capillaries, particularly in metering devices, which is cost-effective to produce and which operates reliably and precisely.

[0013] The microsensor for measuring the position of liquids in capillaries according to the invention is based on the principle of conductivity measurements. However, only a change in the conductivity is essential to the measurement principle. The absolute value of the conductivity of the operating liquid plays a minor role.

[0014] Contained in the capillary is a gas bubble which is enclosed on both sides by the operating solution and which can be moved back and forth within the capillary by means of a sensor chip. A nonconductive liquid which is immiscible with the operating solution may be used instead of the gas bubble. The following description relates only to a bubble, without limiting the universality. It is essential that a significant difference in conductivity exists between the operating liquid and the contents of the bubble. It is also conceivable, therefore, that the operating liquid is nonconductive and the bubble is composed of a conductive liquid. Thus, there is at least one boundary between two different conductivities of the capillary filling in the region above the sensor element.

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[0015] The sensor chip comprises a substrate preferably made of silicon, glass, or plastic. Microstructured, partially passivated metal electrodes preferably made of platinum, iridium, or gold are mounted on the sensor chip. Iridium is characterized by an especially low polarization resistance in aqueous solution. The electrodes each comprise a preferably constant number of partial electrodes which are separated by a preferably constant distance from one another and which are networked with electrical connections. The partial electrodes of preferably two electrodes are positioned pairwise opposite one another, separated preferably by a constant distance, as partial electrode pairs. The recurring basic geometry (meander) thus comprises preferably two electrode pairs, which in turn comprise partial electrode pairs. This basic geometry repeats itself periodically over the entire length of the sensor chip. The distance between the partial electrode pairs in the longitudinal direction, that is, in the direction of the bubble motion to be measured, is always the same. This also applies to adjacent partial electrode pairs which form part of adjacent meanders.

[0016] The electrical connections between the partial electrodes of the electrodes are preferably coated with a passivating layer, whereas the partial electrodes themselves represent the sensor-active regions of the sensor chip and thus are situated directly on the surface, which comes into contact with the operating liquid. The sensor is mounted laterally on the capillary, which is made of glass or plastic, for example, in such a way that the active regions of the electrodes, and thus of the partial electrodes, are located in the interior of the capillary. In contrast, the connections (bondpads) of the electrodes of individual meanders are situated

outside the capillary. To this end, the capillary wall is partially replaced by the sensor chip. When a conductive liquid is present in the capillary and a voltage is applied thereto, a current flows between the oppositely situated partial electrodes of a meander. The impedance of the meander is determined by the wetted electrode area, that is, the number of wetted partial electrode pairs. The impedance decreases with an increasingly wetted area. This effect can be used to advantage in detecting the position of an air bubble, or a conductivity boundary in general, which completely or partially covers the meander, or, in the case of a single conductivity boundary, which is located above the meander. The following discussion relates to a description of the operating mode of the sensor with regard to a bubble, without limiting the universality. Moreover, the discussion is also valid for the presence of a single conductivity boundary. Hence, it is not a bubble position that is determined, but rather, the location of the conductivity boundary between two partial electrode pairs of a meander, or the location of the conductivity boundary between two meanders. A bubble represents a special case in which two conductivity boundaries are present in the capillary filling.

[0017] The position of the bubble may be determined by comparing resistance values of all meanders in the idle state. Regardless of the specific operating liquid, all the meanders wetted by the liquid have the same minimum resistance. When the bubble is large enough to completely cover at least one meander, this results in a maximum resistance value for this meander. The adjoining meanders, which are only partially covered, have intermediate resistance values. To determine the exact position of the liquid surface in the intermediate region of a meander, it is necessary

to know the shape of the resistance curve (reference resistance curve) for a coated meander as well as the minimum and maximum resistance of the affected meander. By interpolating on the curve of a known shape and with the known minimum and maximum values, any intermediate resistance value can then be assigned to a specific partial electrode pair of the corresponding meander, and the position of the bubble or of the conductivity boundary can thus be precisely determined.

[0018] If the wetting properties of the operating liquid with respect to the sensor element are such that no permanent liquid film forms on the sensor element, and if the migration velocity of the bubble is not too high, characteristic abrupt changes in the resistance (jumps) occur during the movement of the bubble over the partial electrode pairs of a meander. In the case of an aqueous solution, this signifies a hydrophobic surface on the sensor element; however, the solution must not be repelled so strongly that no wetting can take place in the regions of the sensor element that are covered by the operating liquid. Ideally, the sensor element is always wetted by the operating liquid in the exact location where it is covered by the operating liquid level. If all meanders are monitored in parallel, the path distance traveled by the bubble, and thus the displaced liquid volume, can be determined from the total number of jumps during migration of the bubble.

[0019] Two possible methods for detecting the position of the bubble can be derived from the behavior of the impedance of the meander:

[0020] In the dynamic method (incremental measurement), the resistance between the electrode pairs of all meanders of the filling level sensor is determined in parallel with many measured values per unit time (high sampling rate). In this manner, the

number of jumps occurring during the movement of the bubble can be counted. Since the distance between the partial electrode pairs in the longitudinal direction is known, the path length traveled by the bubble in the capillary may be determined, and from this value, together with the cross section of the capillary, the displaced liquid volume may be determined. This measurement technique is quasi-digital in nature. The resistance curve is qualitatively evaluated, and the absolute value of the resistance is not used in the evaluation. The conductivity of the operating liquid, which is influenced by a number of factors such as the ion concentration and mobility as well as the temperature, plays a minor role in the measurement result. The conductivity need only be high enough to allow the jumps to be detected.

[0021] In the static method (absolute measurement), the resistance between the electrode pairs of the meanders is measured in the idle state. All meanders that are completely covered by the liquid present in the capillary have a minimum resistance value. If one of the meanders is completely covered by the bubble, said meander has a maximum resistance value. If the adjoining meanders are only partially covered by the bubble, intermediate values appear. When the resistance is qualitatively known (reference resistance curve) as a function of the number of partial electrode pairs (short-circuited partial electrodes) of a meander covered by liquid, and the minimum and maximum values are available, the position of the bubble front over the corresponding meander can be obtained by interpolation of the intermediate values. The displaced liquid volume is again obtained from the distance traveled by the bubble. If the liquid film below the bubble tears cleanly so that all partial electrode pairs that are covered by the bubble are uncovered, the maximum

resistance of the meander that is completely covered by the air bubble is a constant value, independent of the properties of the operating solution or liquid. Since the minimum resistance of a meander that is completely covered by liquid can be redetermined at any time, there is an option for in situ calibration, which is understood to mean calibration performed during operation. However, it is preferable for the same liquid to be present on both sides of the bubble. Here as well, the measuring technique is independent of the conductivity of the operating solution, provided that this conductivity exceeds the minimum value required for measurement.

[0022] A significant advantage of the static, as opposed to the dynamic, measurement method is that the position of the bubble is precisely determined both before and after the metering operation.

[0023] Operations can therefore be performed when high bubble migration velocities are present, since the occurrence of jumps is not important for the measurement. In the dynamic measurement method, the migration velocity of the bubble is limited by the wetting properties of the operating liquid.

[0024] In a preferred embodiment, the meanders are divided into not substantially more than 10 partial electrode pairs. If this number is significantly exceeded, the jumps in conductivity become increasingly difficult to distinguish from one another, especially when the dynamic measurement method is used. This represents a major advantage of the periodic electrode structure, in addition to the possibility for detecting the bubble position for exactly one meander.

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[0025] With regard to bubble size, the bubble should be able to completely cover at least one meander, particularly for the static measurement method. The length of the bubble is preferably twice the length of a meander, thereby ensuring that there is always a meander that is completely covered by the bubble.

[0026] Errors, such as plugging of the capillary, are known in both methods.

[0027] The resolution of the sensor is determined by the number of meanders per unit length of sensor chip and the number of partial electrode pairs per meander. The distance between the partial electrode pairs in the longitudinal direction and the cross section of the capillary define the minimum detectable output or intake of liquid volume.

[0028] When a direct current is supplied to the meanders, undesirable electrochemical effects in the operating liquid may occur at the electrodes. Therefore, alternating current in the kilohertz range is preferably applied to the electrodes. For the conductivity measurement, an alternating current ranging up to 100 millivolts is applied and the resulting current is measured as the output signal.

[0029] The sensor chip according to the invention is characterized by particularly cost-effective production. In addition, the sensor chip allows the position of the liquid surface to be easily and precisely measured. The sensor according to the invention enables the liquid level in capillaries to be electrically measured, which is particularly advantageous in the pipetting of liquids. Furthermore, the measurement of the position of the conductivity boundaries can be used to determine differential pressures, similar to the classic manometer in which the pressure differential creates a difference in levels between the two arms of a U-shaped tube. The capillary in this

case corresponds to the tube. In general, the sensor according to the invention can detect the motion of various liquids in a fluid system in which the liquids are being processed and/or analyzed.

BRIEF DESCRIPTION OF THE DRAWINGS

[0030] The present invention is described hereinafter in more detail, based on embodiment examples and with reference to the drawings, without limiting the general concept of the invention.

[0031] Figure 1 schematically shows the cross section through a capillary (1) with a laterally mounted sensor chip (2) which has microstructured metal electrodes (3).

[0032] Figure 2 shows a section of a sensor according to the invention with a possible electrode geometry in a top view.

[0033] Figure 3 shows how the movement of an air bubble (9) over the meander structure (8) successively covers the partial electrode pairs (11) of the meander and then exposes same.

[0034] Figure 4 shows a typical current curve resulting from the bubble movement in Figure 3 when a meander is supplied with alternating current.

[0035] Figure 5 shows a time plot of the current curves for three adjacent meanders as the result of movement of a bubble over the three meanders.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

[0036] Figure 1 shows a schematic cross section through a capillary (1) made of glass, for example, with a laterally mounted sensor chip (2) having microstructured metal electrodes (3), which represents the preferred design for a pipette with a filling

level sensor. The sensor chip preferably comprises a silicon substrate on which platinum electrodes are mounted.

[0037] Figure 2 shows a section of a sensor according to the invention with a possible electrode geometry in a top view. The active, uncovered regions (5) of the electrodes are located inside the capillary (1) and are distributed over the entire length of the chip. The electrode structure is defined by a continuously recurring configuration. Each electrode comprises a plurality of sensor-active partial electrodes (5), with an electrode pair (meander) (8) always being formed by two electrodes The partial electrodes of the electrode pairs are positioned opposite one another as partial electrode pairs (11). Each electrode has its own electrical connection option (bondpad) (4). Successive meanders are configured so that the distance between the partial electrode pairs (11) is always constant over the entire length of the chip. Each meander comprises two metal electrodes having eight partial electrode pairs which are positioned opposite one another. The individual partial electrodes on each side of a meander are connected in series. The electrical connection between the individual partial electrodes on one side of the meander has an ohmic resistance which must not be too small. In the represented embodiment, the resistance is increased by lengthening the connection in a serpentine shape (7). The distance between adjacent partial electrode pairs (11) in the longitudinal direction is always the same. The distance between partial electrodes in the longitudinal direction is preferably several 10 μm. The smaller the distance between the partial electrode pairs in the longitudinal direction, the higher the resolution of the sensor; that is, the smaller the quantity of liquid that can be metered. The uncovered, active electrode

regions can come into contact with a liquid inside the capillary. The leads to the bondpads situated outside the capillary are covered by a passivation layer (6).

[0038] Figure 3 shows the movement of an air bubble (9) over a meander structure as the air bubble successively covers the individual partial electrode pairs (11) of the meander and then exposes same. A conductive liquid (10) encloses an air bubble, which moves upward on both sides (indicated by an arrow). As soon as the forward front (12) of the bubble uncovers the bottommost partial electrode pair (Figure 3a), the current between the opposing electrodes of the meander drops. The current reaches a minimum when the bubble completely covers the meander (Figure 3b) and then gradually increases again as the bubble migrates across the meander (Figure 3c). The current reaches its initial value after the rear front (13) of the bubble has crossed the topmost partial electrode pair of the meander.

[0039] Figure 4 plots over time the curve of the amplified output signal (current) of a meander which has eight partial electrode pairs. The positions of the bubble in Figures 3a through 3c are assigned to the corresponding locations on the curve. Each time that the bubble front reaches another partial electrode pair, the wetted electrode area makes an abrupt change. As a result, the current curve likewise undergoes abrupt changes (jumps) (14). The degree of distinctiveness of these jumps depends on the wetting properties of the sensor surface between the electrodes. If the sensor surface is hydrophobic, the liquid film underneath the bubble immediately tears and the electrical contact between the oppositely situated partial electrodes is abruptly disconnected, creating a peak. If the chip surface is hydrophilic, a thin liquid film partially remains underneath the bubble. The peak fades

and a plateau is formed. As the velocity of the bubble increases, tearing of the liquid film is retarded, especially at the forward front of the bubble. This results in smoothing of the output signal, with plateaus likewise being formed. The indeterminate tearing behavior of the liquid film underneath the bubble is responsible for the complex shape of the curve maximum with additional small peaks. With high bubble migration velocities, a hydrophilic surface, and a low measurement frequency, the jumps become increasingly difficult to detect. The jumps may be completely obliterated in the curve.

[0040] The shape of the signal is independent of the direction of motion of the bubble. For identical air bubbles, the curve resulting from upward motion as well as the curve resulting from downward motion may be reproduced as often as desired.

[0041] Figure 5 represents a plot over time of the output signals, denoted by (15), (16), and (17), of three adjacent meanders during the movement of a bubble at constant velocity over the meanders. The measurement was made in parallel; that is, the output signals of the three meanders were recorded simultaneously. The figure illustrates the advantage of measuring the position of the bubble by detecting jumps in the current curve. Thus, the maximum absolute values, for example, of the meander output signals where there is complete liquid coverage need not be absolutely identical. In spite of different absolute values of the current, for example between curves 15 and 16, the position of the bubble can be precisely determined by counting.

10/088200
JC13 Rec'd PCT/PTO 15 MAR 2002

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TITLE OF THE INVENTION

Microsensor for Measuring the Position of Liquids in Capillaries

BACKGROUND AND SUMMARY OF THE INVENTION

[0001] This application claims the priority of German Application No. 199 44 331.5, filed, September 15, 1999 and International Application No. PCT/DE00/02609, filed August 3, 2000, the disclosures of which are expressly incorporated by reference herein.

[0002] The invention relates to a microsensor for measuring the position of liquids in capillaries which is particularly well suited for use in automated pipetting dispensers in medical laboratories and in the pharmaceutical industry.

[0003] In the analysis of clinical profiles or routine health checks, modern medicine increasingly relies on the quantitative determination of relevant substances in bodily fluids. The number of substances to be monitored is constantly growing, as is likewise the frequency of testing. Performing greater numbers of analyses while simultaneously lowering costs primarily requires a decrease in the use of reagents, which are often very costly. The tendency toward precise metering of the smallest possible quantities of liquids, with a volumetric range of 0.1 to 20 µL, is therefore a key objective.

[0004] In the metering operation, defined quantities of samples and reagents from starting containers must be distributed onto microtiter plates having many individual reaction receptacles (wells). A conventional plastic microtiter plate contains 96 wells, for example, each with a volume of 500 µL, in a 9-mm grid. Modern pipetting

systems can meter between one and several hundred µL of a liquid, using stepping motor-driven injection pumps, with a piston injection precision of several percent. Typically, eight separately controllable pipettes are arranged in parallel, with the result that a microtiter plate must be filled in several passes. The throughput is therefore limited, which affects the measuring results in kinetic tests. Devices currently exist which contain 96 pipettes. However, such devices are not separately controllable; that is, with each metering operation the same quantity is dispensed to all the pipettes. In many applications, separate control of the pipettes would be preferable. In order to meter quantities of liquids from 0.1 to 20 µL with greater precision in an array of separately controllable pipettes, the metering operation must be actively monitored at each individual pipette.

[0005] In the course of a quantitative analysis, samples and reagents are successively pipetted into the appropriate wells of the microtiter plate, using an injection pump via a liquid column. The operating liquid is typically separated from the sample or reagent by an air bubble to avoid contamination. After the reactions have taken place in the wells, the concentration of one of the reaction products is photometrically determined, and the concentration of the sample component being sought is calculated therefrom.

[0006] The sample volume dispensed during a pipetting operation results from the piston feed from the injection pump. However, the sample volume is defined in the same manner both before and after the metering operation by the filling level of the sample liquid in the pipette.

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[Description of the Prior Art]

[0007] Filling level sensors for monitoring liquids in reservoirs or tanks have been known for quite some time. In addition to sensors that are based on floats, there are a number of systems with no moving parts. Such systems are based, for example, on optical or electrical measurement techniques.

[0008] U.S. Patent 5,138,880 describes a capacitive sensor comprising two concentric cylinders which are submerged in a dielectric medium along the measurement axis. The cylinders are divided into a number of discrete condensers. The capacitance of each individual condenser depends on whether air or the medium to be monitored is present between the electrodes. By comparison of the capacitances, the filling height of the medium in the container may be quasi-digitally determined with a precision corresponding to the number of measurement segments. The capacitive measurement principle can also be employed in the form of a planar sensor. This type of sensor must be calibrated for each liquid.

[0009] The filling level may be potentiometrically determined in conductive liquids. A rod-shaped resistor, which is vertically submerged in the liquid and together with this liquid forms the resistors of a bridge circuit, may serve as the measuring probe. The voltage drop at the resistor, measured via the liquid, is proportional to the liquid level. An example of such is disclosed in U.S. Patent 5,146,785. Here, the measuring probe is additionally divided into a series of individual resistors, thus generating a stair-step, quasi-digital output signal.

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[0010] A further electrical sensor principle is based on conductivity measurements. To this end, an alternating current in the kHz range is applied between two respective electrodes, and the current between the electrode pairs is measured. An example of such is disclosed in U.S. Patent 5,719,556.

[0011] The electrical devices for measuring liquid levels according to the current art are not suited for measuring the position of liquids in capillaries. The use of said devices is limited to the measurement of filling levels in tanks, for example.

[Object of the Invention]

[0012] The object of the invention is to provide a device and a method for operating said device for electrically measuring the position of liquid levels in capillaries, particularly in metering devices, which is cost-effective to produce and which operates reliably and precisely.

[Description

[0013] The object of the present invention is achieved by the features of Claim 1. The present invention further provides a method for operating a sensor in Claims 11 through 17.

[0014] The preferred embodiments are the subject of the subclaims.]

[0015] The microsensor for measuring the position of liquids in capillaries according to the invention is based on the principle of conductivity measurements. However, only a change in the conductivity is essential to the measurement principle. The absolute value of the conductivity of the operating liquid plays a minor role.

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[0016] Contained in the capillary is a gas bubble which is enclosed on both sides by the operating solution and which can be moved back and forth within the capillary by means of a sensor chip. A nonconductive liquid which is immiscible with the operating solution may be used instead of the gas bubble. The following description relates only to a bubble, without limiting the universality. It is essential that a significant difference in conductivity exists between the operating liquid and the contents of the bubble. It is also conceivable, therefore, that the operating liquid is nonconductive and the bubble is composed of a conductive liquid. Thus, there is at least one boundary between two different conductivities of the capillary filling in the region above the sensor element.

[0017] The sensor chip comprises a substrate preferably made of silicon, glass, or plastic. Microstructured, partially passivated metal electrodes preferably made of platinum, iridium, or gold are mounted on the sensor chip. Iridium is characterized by an especially low polarization resistance in aqueous solution. The electrodes each comprise a preferably constant number of partial electrodes which are separated by a preferably constant distance from one another and which are networked with electrical connections. The partial electrodes of preferably two electrodes are positioned pairwise opposite one another, separated preferably by a constant distance, as partial electrode pairs. The recurring basic geometry (meander) thus comprises preferably two electrode pairs, which in turn comprise partial electrode pairs. This basic geometry repeats itself periodically over the entire length of the sensor chip. The distance between the partial electrode pairs in the longitudinal

direction, that is, in the direction of the bubble motion to be measured, is always the same. This also applies to adjacent partial electrode pairs which form part of adjacent meanders.

[0018] The electrical connections between the partial electrodes of the electrodes are preferably coated with a passivating layer, whereas the partial electrodes themselves represent the sensor-active regions of the sensor chip and thus are situated directly on the surface, which comes into contact with the operating liquid. The sensor is mounted laterally on the capillary, which is made of glass or plastic, for example, in such a way that the active regions of the electrodes, and thus of the partial electrodes, are located in the interior of the capillary. In contrast, the connections (bondpads) of the electrodes of individual meanders are situated outside the capillary. To this end, the capillary wall is partially replaced by the sensor chip. When a conductive liquid is present in the capillary and a voltage is applied thereto, a current flows between the oppositely situated partial electrodes of a meander. The impedance of the meander is determined by the wetted electrode area, that is, the number of wetted partial electrode pairs. The impedance decreases with an increasingly wetted area. This effect can be used to advantage in detecting the position of an air bubble, or a conductivity boundary in general, which completely or partially covers the meander, or, in the case of a single conductivity boundary, which is located above the meander. The following discussion relates to a description of the operating mode of the sensor with regard to a bubble, without limiting the universality. Moreover, the discussion is also valid for the presence of a

single conductivity boundary. Hence, it is not a bubble position that is determined, but rather, the location of the conductivity boundary between two partial electrode pairs of a meander, or the location of the conductivity boundary between two meanders. A bubble represents a special case in which two conductivity boundaries are present in the capillary filling.

[0019] The position of the bubble may be determined by comparing resistance values of all meanders in the idle state. Regardless of the specific operating liquid, all the meanders wetted by the liquid have the same minimum resistance. When the bubble is large enough to completely cover at least one meander, this results in a maximum resistance value for this meander. The adjoining meanders, which are only partially covered, have intermediate resistance values. To determine the exact position of the liquid surface in the intermediate region of a meander, it is necessary to know the shape of the resistance curve (reference resistance curve) for a coated meander as well as the minimum and maximum resistance of the affected meander. By interpolating on the curve of a known shape and with the known minimum and maximum values, any intermediate resistance value can then be assigned to a specific partial electrode pair of the corresponding meander, and the position of the bubble or of the conductivity boundary can thus be precisely determined.

[0020] If the wetting properties of the operating liquid with respect to the sensor element are such that no permanent liquid film forms on the sensor element, and if the migration velocity of the bubble is not too high, characteristic abrupt changes in the resistance (jumps) occur during the movement of the bubble over the partial

electrode pairs of a meander. In the case of an aqueous solution, this signifies a hydrophobic surface on the sensor element; however, the solution must not be repelled so strongly that no wetting can take place in the regions of the sensor element that are covered by the operating liquid. Ideally, the sensor element is always wetted by the operating liquid in the exact location where it is covered by the operating liquid level. If all meanders are monitored in parallel, the path distance traveled by the bubble, and thus the displaced liquid volume, can be determined from the total number of jumps during migration of the bubble.

[0021] Two possible methods for detecting the position of the bubble can be derived from the behavior of the impedance of the meander:

[0022] In the dynamic method (incremental measurement), the resistance between the electrode pairs of all meanders of the filling level sensor is determined in parallel with many measured values per unit time (high sampling rate). In this manner, the number of jumps occurring during the movement of the bubble can be counted. Since the distance between the partial electrode pairs in the longitudinal direction is known, the path length traveled by the bubble in the capillary may be determined, and from this value, together with the cross section of the capillary, the displaced liquid volume may be determined. This measurement technique is quasi-digital in nature. The resistance curve is qualitatively evaluated, and the absolute value of the resistance is not used in the evaluation. The conductivity of the operating liquid, which is influenced by a number of factors such as the ion concentration and mobility

as well as the temperature, plays a minor role in the measurement result. The conductivity need only be high enough to allow the jumps to be detected.

[0023] In the static method (absolute measurement), the resistance between the electrode pairs of the meanders is measured in the idle state. All meanders that are completely covered by the liquid present in the capillary have a minimum resistance value. If one of the meanders is completely covered by the bubble, said meander has a maximum resistance value. If the adjoining meanders are only partially covered by the bubble, intermediate values appear. When the resistance is qualitatively known (reference resistance curve) as a function of the number of partial electrode pairs (short-circuited partial electrodes) of a meander covered by liquid, and the minimum and maximum values are available, the position of the bubble front over the corresponding meander can be obtained by interpolation of the intermediate values. The displaced liquid volume is again obtained from the distance traveled by the bubble. If the liquid film below the bubble tears cleanly so that all partial electrode pairs that are covered by the bubble are uncovered, the maximum resistance of the meander that is completely covered by the air bubble is a constant value, independent of the properties of the operating solution or liquid. Since the minimum resistance of a meander that is completely covered by liquid can be redetermined at any time, there is an option for in situ calibration, which is understood to mean calibration performed during operation. However, it is preferable for the same liquid to be present on both sides of the bubble. Here as well, the measuring technique is independent of the conductivity of the operating solution,

provided that this conductivity exceeds the minimum value required for measurement.

[0024] A significant advantage of the static, as opposed to the dynamic, measurement method is that the position of the bubble is precisely determined both before and after the metering operation.

[0025] Operations can therefore be performed when high bubble migration velocities are present, since the occurrence of jumps is not important for the measurement. In the dynamic measurement method, the migration velocity of the bubble is limited by the wetting properties of the operating liquid.

[0026] In a preferred embodiment, the meanders are divided into not substantially more than 10 partial electrode pairs. If this number is significantly exceeded, the jumps in conductivity become increasingly difficult to distinguish from one another, especially when the dynamic measurement method is used. This represents a major advantage of the periodic electrode structure, in addition to the possibility for detecting the bubble position for exactly one meander.

[0027] With regard to bubble size, the bubble should be able to completely cover at least one meander, particularly for the static measurement method. The length of the bubble is preferably twice the length of a meander, thereby ensuring that there is always a meander that is completely covered by the bubble.

[0028] Errors, such as plugging of the capillary, are known in both methods.

[0029] The resolution of the sensor is determined by the number of meanders per unit length of sensor chip and the number of partial electrode pairs per meander. The

distance between the partial electrode pairs in the longitudinal direction and the cross section of the capillary define the minimum detectable output or intake of liquid volume.

[0030] When a direct current is supplied to the meanders, undesirable electrochemical effects in the operating liquid may occur at the electrodes. Therefore, alternating current in the kilohertz range is preferably applied to the electrodes. For the conductivity measurement, an alternating current ranging up to 100 millivolts is applied and the resulting current is measured as the output signal.

[0031] The sensor chip according to the invention is characterized by particularly cost-effective production. In addition, the sensor chip allows the position of the liquid surface to be easily and precisely measured. The sensor according to the invention enables the liquid level in capillaries to be electrically measured, which is particularly advantageous in the pipetting of liquids. Furthermore, the measurement of the position of the conductivity boundaries can be used to determine differential pressures, similar to the classic manometer in which the pressure differential creates a difference in levels between the two arms of a U-shaped tube. The capillary in this case corresponds to the tube. In general, the sensor according to the invention can detect the motion of various liquids in a fluid system in which the liquids are being processed and/or analyzed.

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BRIEF DESCRIPTION OF THE DRAWINGS

[0032] The present invention is described hereinafter in more detail, based on embodiment examples and with reference to the drawings, without limiting the general concept of the invention.

[0033] Figure 1 schematically shows the cross section through a capillary (1) with a laterally mounted sensor chip (2) which has microstructured metal electrodes (3).

[0034] Figure 2 shows a section of a sensor according to the invention with a possible electrode geometry in a top view.

[0035] Figure 3 shows how the movement of an air bubble (9) over the meander structure (8) successively covers the partial electrode pairs (11) of the meander and then exposes same.

[0036] Figure 4 shows a typical current curve resulting from the bubble movement in Figure 3 when a meander is supplied with alternating current.

[0037] Figure 5 shows a time plot of the current curves for three adjacent meanders as the result of movement of a bubble over the three meanders.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

[0038] Figure 1 shows a schematic cross section through a capillary (1) made of glass, for example, with a laterally mounted sensor chip (2) having microstructured metal electrodes (3), which represents the preferred design for a pipette with a filling level sensor. The sensor chip preferably comprises a silicon substrate on which platinum electrodes are mounted.

[0039] Figure 2 shows a section of a sensor according to the invention with a possible electrode geometry in a top view. The active, uncovered regions (5) of the electrodes are located inside the capillary (1) and are distributed over the entire length of the chip. The electrode structure is defined by a continuously recurring configuration. Each electrode comprises a plurality of sensor-active partial electrodes (5), with an electrode pair (meander) (8) always being formed by two electrodes The partial electrodes of the electrode pairs are positioned opposite one another as partial electrode pairs (11). Each electrode has its own electrical connection option (bondpad) (4). Successive meanders are configured so that the distance between the partial electrode pairs (11) is always constant over the entire length of the chip. Each meander comprises two metal electrodes having eight partial electrode pairs which are positioned opposite one another. The individual partial electrodes on each side of a meander are connected in series. The electrical connection between the individual partial electrodes on one side of the meander has an ohmic resistance which must not be too small. In the represented embodiment, the resistance is increased by lengthening the connection in a serpentine shape (7). The distance between adjacent partial electrode pairs (11) in the longitudinal direction is always the same. The distance between partial electrodes in the longitudinal direction is preferably several 10 μm. The smaller the distance between the partial electrode pairs in the longitudinal direction, the higher the resolution of the sensor; that is, the smaller the quantity of liquid that can be metered. The uncovered, active electrode

regions can come into contact with a liquid inside the capillary. The leads to the bondpads situated outside the capillary are covered by a passivation layer (6).

[0040] Figure 3 shows the movement of an air bubble (9) over a meander structure as the air bubble successively covers the individual partial electrode pairs (11) of the meander and then exposes same. A conductive liquid (10) encloses an air bubble, which moves upward on both sides (indicated by an arrow). As soon as the forward front (12) of the bubble uncovers the bottommost partial electrode pair (Figure 3a), the current between the opposing electrodes of the meander drops. The current reaches a minimum when the bubble completely covers the meander (Figure 3b) and then gradually increases again as the bubble migrates across the meander (Figure 3c). The current reaches its initial value after the rear front (13) of the bubble has crossed the topmost partial electrode pair of the meander.

[0041] Figure 4 plots over time the curve of the amplified output signal (current) of a meander which has eight partial electrode pairs. The positions of the bubble in Figures 3a through 3c are assigned to the corresponding locations on the curve. Each time that the bubble front reaches another partial electrode pair, the wetted electrode area makes an abrupt change. As a result, the current curve likewise undergoes abrupt changes (jumps) (14). The degree of distinctiveness of these jumps depends on the wetting properties of the sensor surface between the electrodes. If the sensor surface is hydrophobic, the liquid film underneath the bubble immediately tears and the electrical contact between the oppositely situated partial electrodes is abruptly disconnected, creating a peak. If the chip surface is

hydrophilic, a thin liquid film partially remains underneath the bubble. The peak fades and a plateau is formed. As the velocity of the bubble increases, tearing of the liquid film is retarded, especially at the forward front of the bubble. This results in smoothing of the output signal, with plateaus likewise being formed. The indeterminate tearing behavior of the liquid film underneath the bubble is responsible for the complex shape of the curve maximum with additional small peaks. With high bubble migration velocities, a hydrophilic surface, and a low measurement frequency, the jumps become increasingly difficult to detect. The jumps may be completely obliterated in the curve.

[0042] The shape of the signal is independent of the direction of motion of the bubble. For identical air bubbles, the curve resulting from upward motion as well as the curve resulting from downward motion may be reproduced as often as desired.

[0043] Figure 5 represents a plot over time of the output signals, denoted by (15), (16), and (17), of three adjacent meanders during the movement of a bubble at constant velocity over the meanders. The measurement was made in parallel; that is, the output signals of the three meanders were recorded simultaneously. The figure illustrates the advantage of measuring the position of the bubble by detecting jumps in the current curve. Thus, the maximum absolute values, for example, of the meander output signals where there is complete liquid coverage need not be absolutely identical. In spite of different absolute values of the current, for example between curves 15 and 16, the position of the bubble can be precisely determined by counting.

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JC13 Rec'd PCT/PTO 15 MAR 2002

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Microsensor for Measuring the Position of Liquids in Capillaries

The invention relates to a microsensor for measuring the position of liquids in capillaries which is particularly well suited for use in automated pipetting dispensers in medical laboratories and in the pharmaceutical industry.

In the analysis of clinical profiles or routine health checks, modern medicine increasingly relies on the quantitative determination of relevant substances in bodily fluids. The number of substances to be monitored is constantly growing, as is likewise the frequency of testing. Performing greater numbers of analyses while simultaneously lowering costs primarily requires a decrease in the use of reagents, which are often very costly. The tendency toward precise metering of the smallest possible quantities of liquids, with a volumetric range of 0.1 to 20 μL, is therefore a key objective.

In the metering operation, defined quantities of samples and reagents from starting containers must be distributed onto microtiter plates having many individual reaction receptacles (wells). A conventional plastic microtiter plate contains 96 wells, for example, each with a volume of 500 μL, in a 9-mm grid. Modern pipetting systems can meter between one and several hundred μL of a liquid, using stepping motor-driven injection pumps, with a piston injection precision of several percent. Typically, eight separately controllable pipettes are arranged in parallel, with the result that a microtiter plate must be filled in several passes. The throughput is therefore limited, which affects the measuring results in kinetic tests. Devices currently exist which contain 96 pipettes. However, such devices are not separately controllable; that is, with each metering operation the same quantity is dispensed to all the pipettes. In many applications, separate control of the pipettes would be preferable. In order to meter quantities of liquids from 0.1 to 20 μL with greater precision in an array of separately controllable pipettes,

the metering operation must be actively monitored at each individual pipette.

In the course of a quantitative analysis, samples and reagents are successively pipetted into the appropriate wells of the microtiter plate, using an injection pump via a liquid column. The operating liquid is typically separated from the sample or reagent by an air bubble to avoid contamination. After the reactions have taken place in the wells, the concentration of one of the reaction products is photometrically determined, and the concentration of the sample component being sought is calculated therefrom.

The sample volume dispensed during a pipetting operation results from the piston feed from the injection pump. However, the sample volume is defined in the same manner both before and after the metering operation by the filling level of the sample liquid in the pipette.

Description of the Prior Art

Filling level sensors for monitoring liquids in reservoirs or tanks have been known for quite some time. In addition to sensors that are based on floats, there are a number of systems with no moving parts. Such systems are based, for example, on optical or electrical measurement techniques.

U.S. Patent 5,138,880 describes a capacitive sensor comprising two concentric cylinders which are submerged in a dielectric medium along the measurement axis. The cylinders are divided into a number of discrete condensers. The capacitance of each individual condenser depends on whether air or the medium to be monitored is present between the electrodes. By comparison of the capacitances, the filling height of the medium in the container may be quasi-digitally determined with a precision corresponding to the number of measurement segments. The capacitive measurement principle can also be employed in the form of a planar sensor. This type of sensor must be calibrated for each liquid.

The filling level may be potentiometrically determined in conductive liquids. A rod-shaped resistor, which is vertically submerged in the liquid and together with this liquid forms the resistors of a bridge circuit, may serve as the measuring probe. The voltage drop at the resistor, measured via the liquid, is proportional to the liquid level. An example of such is disclosed in U.S. Patent 5,146,785. Here, the measuring probe is additionally divided into a series of individual resistors, thus generating a stair-step, quasi-digital output signal.

A further electrical sensor principle is based on conductivity measurements. To this end, an alternating current in the kHz range is applied between two respective electrodes, and the current between the electrode pairs is measured. An example of such is disclosed in U.S. Patent 5,719,556.

The electrical devices for measuring liquid levels according to the current art are not suited for measuring the position of liquids in capillaries. The use of said devices is limited to the measurement of filling levels in tanks, for example.

Object of the Invention

The object of the invention is to provide a device and a method for operating said device for electrically measuring the position of liquid levels in capillaries, particularly in metering devices, which is cost-effective to produce and which operates reliably and precisely.

Description

The object of the present invention is achieved by the features of Claim 1. The present invention further provides a method for operating a sensor in Claims 11 through 17.

The preferred embodiments are the subject of the subclaims.

The microsensor for measuring the position of liquids in capillaries according to the invention is based on the principle of conductivity measurements. However, only a change in the conductivity is essential to the measurement principle. The absolute value of the conductivity of the operating liquid plays a minor role.

Contained in the capillary is a gas bubble which is enclosed on both sides by the operating solution and which can be moved back and forth within the capillary by means of a sensor chip. A nonconductive liquid which is immiscible with the operating solution may be used instead of the gas bubble. The following description relates only to a bubble, without limiting the universality. It is essential that a significant difference in conductivity exists between the operating liquid and the contents of the bubble. It is also conceivable, therefore, that the operating liquid is nonconductive and the bubble is composed of a conductive liquid. Thus, there is at least one boundary between two different conductivities of the capillary filling in the region above the sensor element.

The sensor chip comprises a substrate preferably made of silicon, glass, or plastic. Microstructured, partially passivated metal electrodes preferably made of platinum, iridium, or gold are mounted on the sensor chip. Iridium is characterized by an especially low polarization resistance in aqueous solution. The electrodes each comprise a preferably constant number of partial electrodes which are separated by a preferably constant distance from one another and which are networked with electrical connections. The partial electrodes of preferably two electrodes are positioned pairwise opposite one another, separated preferably by a constant distance, as partial electrode pairs. The recurring basic geometry (meander) thus comprises preferably two electrode pairs, which in turn comprise partial electrode pairs. This basic geometry repeats itself periodically over the entire length of the sensor chip. The distance between the partial electrode pairs in the longitudinal direction, that is, in the direction of the bubble motion to be measured, is always the same. This also applies to adjacent partial electrode pairs which form part of adjacent meanders.

The electrical connections between the partial electrodes of the electrodes are preferably coated with a passivating layer, whereas the partial electrodes themselves represent the sensor-active regions of the sensor chip and thus are situated directly on the surface, which comes into contact with the operating liquid. The sensor is mounted laterally on the capillary, which is made of glass or plastic, for example, in such a way that the active regions of the electrodes, and thus of the partial electrodes, are located in the interior of the capillary. In contrast, the connections (bondpads) of the electrodes of individual meanders are situated outside the capillary. To this end, the capillary wall is partially replaced by the sensor chip. When a conductive liquid is present in the capillary and a voltage is applied thereto, a current flows between the oppositely situated partial electrodes of a meander. The impedance of the meander is determined by the wetted electrode area, that is, the number of wetted partial electrode pairs. The impedance decreases with an increasingly wetted area. This effect can be used to advantage in detecting the position of an air bubble, or a conductivity boundary in general, which completely or partially covers the meander, or, in the case of a single conductivity boundary, which is located above the meander. The following discussion relates to a description of the operating mode of the sensor with regard to a bubble, without limiting the universality. Moreover, the discussion is also valid for the presence of a single conductivity boundary. Hence, it is not a bubble position that is determined, but rather, the location of the conductivity boundary between two partial electrode pairs of a meander, or the location of the conductivity boundary between two meanders. A bubble represents a special case in which two conductivity boundaries are present in the capillary filling.

The position of the bubble may be determined by comparing resistance values of all meanders in the idle state. Regardless of the specific operating liquid, all the meanders wetted by the liquid have the same minimum resistance. When the bubble is large enough to completely cover at least one meander, this results in a maximum resistance value for this meander. The adjoining meanders, which are only partially covered, have intermediate resistance values. To determine the exact position of the liquid surface in the intermediate region of a meander, it is

necessary to know the shape of the resistance curve (reference resistance curve) for a coated meander as well as the minimum and maximum resistance of the affected meander. By interpolating on the curve of a known shape and with the known minimum and maximum values, any intermediate resistance value can then be assigned to a specific partial electrode pair of the corresponding meander, and the position of the bubble or of the conductivity boundary can thus be precisely determined.

If the wetting properties of the operating liquid with respect to the sensor element are such that no permanent liquid film forms on the sensor element, and if the migration velocity of the bubble is not too high, characteristic abrupt changes in the resistance (jumps) occur during the movement of the bubble over the partial electrode pairs of a meander. In the case of an aqueous solution, this signifies a hydrophobic surface on the sensor element; however, the solution must not be repelled so strongly that no wetting can take place in the regions of the sensor element that are covered by the operating liquid. Ideally, the sensor element is always wetted by the operating liquid in the exact location where it is covered by the operating liquid level. If all meanders are monitored in parallel, the path distance traveled by the bubble, and thus the displaced liquid volume, can be determined from the total number of jumps during migration of the bubble.

Two possible methods for detecting the position of the bubble can be derived from the behavior of the impedance of the meander:

In the dynamic method (incremental measurement), the resistance between the electrode pairs of all meanders of the filling level sensor is determined in parallel with many measured values per unit time (high sampling rate). In this manner, the number of jumps occurring during the movement of the bubble can be counted. Since the distance between the partial electrode pairs in the longitudinal direction is known, the path length traveled by the bubble in the capillary may be determined, and from this value, together with the cross section of the capillary, the displaced liquid volume may be determined. This measurement technique is quasi-digital in nature. The resistance curve is qualitatively evaluated, and the absolute value of the

resistance is not used in the evaluation. The conductivity of the operating liquid, which is influenced by a number of factors such as the ion concentration and mobility as well as the temperature, plays a minor role in the measurement result. The conductivity need only be high enough to allow the jumps to be detected.

In the static method (absolute measurement), the resistance between the electrode pairs of the meanders is measured in the idle state. All meanders that are completely covered by the liquid present in the capillary have a minimum resistance value. If one of the meanders is completely covered by the bubble, said meander has a maximum resistance value. If the adjoining meanders are only partially covered by the bubble, intermediate values appear. When the resistance is qualitatively known (reference resistance curve) as a function of the number of partial electrode pairs (short-circuited partial electrodes) of a meander covered by liquid, and the minimum and maximum values are available, the position of the bubble front over the corresponding meander can be obtained by interpolation of the intermediate values. The displaced liquid volume is again obtained from the distance traveled by the bubble. If the liquid film below the bubble tears cleanly so that all partial electrode pairs that are covered by the bubble are uncovered, the maximum resistance of the meander that is completely covered by the air bubble is a constant value, independent of the properties of the operating solution or liquid. Since the minimum resistance of a meander that is completely covered by liquid can be redetermined at any time, there is an option for in situ calibration, which is understood to mean calibration performed during operation. However, it is preferable for the same liquid to be present on both sides of the bubble. Here as well, the measuring technique is independent of the conductivity of the operating solution, provided that this conductivity exceeds the minimum value required for measurement.

A significant advantage of the static, as opposed to the dynamic, measurement method is that the position of the bubble is precisely determined both before and after the metering operation.

Operations can therefore be performed when high bubble migration velocities are present, since the occurrence of jumps is not important for the measurement. In the dynamic measurement method, the migration velocity of the bubble is limited by the wetting properties of the operating liquid.

In a preferred embodiment, the meanders are divided into not substantially more than 10 partial electrode pairs. If this number is significantly exceeded, the jumps in conductivity become increasingly difficult to distinguish from one another, especially when the dynamic measurement method is used. This represents a major advantage of the periodic electrode structure, in addition to the possibility for detecting the bubble position for exactly one meander.

With regard to bubble size, the bubble should be able to completely cover at least one meander, particularly for the static measurement method. The length of the bubble is preferably twice the length of a meander, thereby ensuring that there is always a meander that is completely covered by the bubble.

Errors, such as plugging of the capillary, are known in both methods.

The resolution of the sensor is determined by the number of meanders per unit length of sensor chip and the number of partial electrode pairs per meander. The distance between the partial electrode pairs in the longitudinal direction and the cross section of the capillary define the minimum detectable output or intake of liquid volume.

When a direct current is supplied to the meanders, undesirable electrochemical effects in the operating liquid may occur at the electrodes. Therefore, alternating current in the kilohertz range is preferably applied to the electrodes. For the conductivity measurement, an alternating current ranging up to 100 millivolts is applied and the resulting current is measured as the output signal.

The sensor chip according to the invention is characterized by particularly cost-effective production. In addition, the sensor chip allows the position of the liquid surface to be easily and

precisely measured. The sensor according to the invention enables the liquid level in capillaries to be electrically measured, which is particularly advantageous in the pipetting of liquids. Furthermore, the measurement of the position of the conductivity boundaries can be used to determine differential pressures, similar to the classic manometer in which the pressure differential creates a difference in levels between the two arms of a U-shaped tube. The capillary in this case corresponds to the tube. In general, the sensor according to the invention can detect the motion of various liquids in a fluid system in which the liquids are being processed and/or analyzed.

The present invention is described hereinafter in more detail, based on embodiment examples and with reference to the drawings, without limiting the general concept of the invention.

Figure 1 schematically shows the cross section through a capillary (1) with a laterally mounted sensor chip (2) which has microstructured metal electrodes (3).

Figure 2 shows a section of a sensor according to the invention with a possible electrode geometry in a top view.

Figure 3 shows how the movement of an air bubble (9) over the meander structure (8) successively covers the partial electrode pairs (11) of the meander and then exposes same.

Figure 4 shows a typical current curve resulting from the bubble movement in Figure 3 when a meander is supplied with alternating current.

Figure 5 shows a time plot of the current curves for three adjacent meanders as the result of movement of a bubble over the three meanders.

Figure 1 shows a schematic cross section through a capillary (1) made of glass, for example, with a laterally mounted sensor chip (2) having microstructured metal electrodes (3), which represents the preferred design for a pipette with a filling level sensor. The sensor chip preferably comprises a silicon substrate on which platinum electrodes are mounted.

Figure 2 shows a section of a sensor according to the invention with a possible electrode geometry in a top view. The active, uncovered regions (5) of the electrodes are located inside the capillary (1) and are distributed over the entire length of the chip. The electrode structure is defined by a continuously recurring configuration. Each electrode comprises a plurality of sensor-active partial electrodes (5), with an electrode pair (meander) (8) always being formed by two electrodes The partial electrodes of the electrode pairs are positioned opposite one another as partial electrode pairs (11). Each electrode has its own electrical connection option (bondpad) (4). Successive meanders are configured so that the distance between the partial electrode pairs (11) is always constant over the entire length of the chip. Each meander comprises two metal electrodes having eight partial electrode pairs which are positioned opposite one another. The individual partial electrodes on each side of a meander are connected in series. The electrical connection between the individual partial electrodes on one side of the meander has an ohmic resistance which must not be too small. In the represented embodiment, the resistance is increased by lengthening the connection in a serpentine shape (7). The distance between adjacent partial electrode pairs (11) in the longitudinal direction is always the same. The distance between partial electrodes in the longitudinal direction is preferably several 10 μm. The smaller the distance between the partial electrode pairs in the longitudinal direction, the higher the resolution of the sensor; that is, the smaller the quantity of liquid that can be metered. The uncovered, active electrode regions can come into contact with a liquid inside the capillary. The leads to the bondpads situated outside the capillary are covered by a passivation layer (6).

Figure 3 shows the movement of an air bubble (9) over a meander structure as the air bubble successively covers the individual partial electrode pairs (11) of the meander and then exposes same. A conductive liquid (10) encloses an air bubble, which moves upward on both sides (indicated by an arrow). As soon as the forward front (12) of the bubble uncovers the bottommost partial electrode pair (Figure 3a), the current between the opposing electrodes of the meander drops. The current reaches a minimum when the bubble completely covers the meander (Figure 3b) and then gradually increases again

as the bubble migrates across the meander (Figure 3c). The current reaches its initial value after the rear front (13) of the bubble has crossed the topmost partial electrode pair of the meander.

Figure 4 plots over time the curve of the amplified output signal (current) of a meander which has eight partial electrode pairs. The positions of the bubble in Figures 3a through 3c are assigned to the corresponding locations on the curve. Each time that the bubble front reaches another partial electrode pair, the wetted electrode area makes an abrupt change. As a result, the current curve likewise undergoes abrupt changes (jumps) (14). The degree of distinctiveness of these jumps depends on the wetting properties of the sensor surface between the electrodes. If the sensor surface is hydrophobic, the liquid film underneath the bubble immediately tears and the electrical contact between the oppositely situated partial electrodes is abruptly disconnected, creating a peak. If the chip surface is hydrophilic, a thin liquid film partially remains underneath the bubble. The peak fades and a plateau is formed. As the velocity of the bubble increases, tearing of the liquid film is retarded, especially at the forward front of the bubble. This results in smoothing of the output signal, with plateaus likewise being formed. The indeterminate tearing behavior of the liquid film underneath the bubble is responsible for the complex shape of the curve maximum with additional small peaks. With high bubble migration velocities, a hydrophilic surface, and a low measurement frequency, the jumps become increasingly difficult to detect. The jumps may be completely obliterated in the curve.

The shape of the signal is independent of the direction of motion of the bubble. For identical air bubbles, the curve resulting from upward motion as well as the curve resulting from downward motion may be reproduced as often as desired.

Figure 5 represents a plot over time of the output signals, denoted by (15), (16), and (17), of three adjacent meanders during the movement of a bubble at constant velocity over the meanders. The measurement was made in parallel; that is, the output signals of the three meanders were recorded simultaneously. The figure illustrates the advantage of measuring the position of

the bubble by detecting jumps in the current curve. Thus, the maximum absolute values, for example, of the meander output signals where there is complete liquid coverage need not be absolutely identical. In spite of different absolute values of the current, for example between curves 15 and 16, the position of the bubble can be precisely determined by counting.

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Claims

1. Sensor element for electrically measuring the position of liquid levels, comprising

   – a substrate (2) and

   – a plurality of electrodes (3) that can be contacted individually and that are mounted on the substrate, characterized in that the electrodes comprise sensor-active partial electrodes (5) that are networked with electrical connections (7), whereby the partial electrodes of two respective electrodes are always positioned opposite one another, separated by a distance, as partial electrode pairs (11), and the electrode pairs (8) thus formed recur periodically over the length of the sensor.

2. Sensor element according to Claim 1, characterized in that the electrical connections (7) of the networked partial electrodes are coated with a passivating layer (6).

3. Sensor element according to one of Claims 1 or 2, characterized in that the partial electrodes positioned pairwise opposite one another are always separated by the same distance, and/or the distances between the partial electrode pairs in the longitudinal direction of the sensor element are constant over the entire length of the sensor element, and/or the number of partial electrode pairs per electrode pair is constant.

4. Sensor element according to at least one of Claims 1 through 3, characterized in that the distance between the partial electrode pairs in the longitudinal direction is in the range of 100 μm.

5. Sensor element according to at least one of Claims 1 through 4, characterized in that the substrate is made of silicon, glass, or plastic.

6. Sensor element according to at least one of Claims 1 through 5, characterized in that the electrodes are made of platinum, iridium, or gold.

7. Sensor element according to at least one of Claims 1 through 6, characterized in that the sensor chip surface has wetting properties such that the boundaries of the liquid wetting of the sensor surface correspond to the liquid level.

8. Arrangement in which the sensor element according to at least one of Claims 1 through 7 is used for measuring a capillary filling, characterized in that the sensor element is attached to a capillary in such a way that the sensor-active partial electrodes (5) are situated inside the capillary and the electrical connection options are situated outside the capillary, and that at least one conductivity boundary of the capillary filling is located in the region of the sensor element.

9. Arrangement in which the sensor element is used according to at least one of Claims 1 through 7 and Claim 8, characterized in that two conductivity boundaries of operating liquids in the capillary form a bubble in the region of the sensor element, said bubble being bounded on both sides by the operating liquid.

10. Arrangement in which the sensor element is used according to at least one of Claims 1 through 7 and Claims 8 or 9, characterized in that the bubble is filled with gas, and/or the length of the bubble is approximately twice the length of an electrode pair in the longitudinal direction, and/or the same operating liquid is present on both sides of the bubble.

11. Method for measuring liquid levels using the arrangement according to at least one of Claims 1 through 8 and 9 and/or 10, characterized in that it is determined which electrode pairs are covered and which are not covered by the operating liquid by measuring the resistance of each individual electrode pair in the idle state of the operating liquid and comparing the resistance values to the characteristic minimum and maximum values for liquid coverage or no liquid coverage, and from this information the position of the conductivity boundary or of the bubble on a specific electrode pair is detected.

12. Method for measuring liquid levels using the arrangement according to at least one of Claims 1 through 8 and 9 and/or 10, characterized in that the position of a conductivity boundary within an electrode pair in the idle state of the operating liquid is determined

by comparing the intermediate value lying between the minimum and maximum resistance value of the electrode pair to a reference resistance curve of the electrode pair, and the position of the conductivity boundary for a specific partial electrode pair is thereby obtained.

13. Method according to at least one of Claims 11 or 12, characterized in that the path distance traveled by the bubble is determined from the detected position of the bubble or of the conductivity boundary before and after movement of the bubble.

14. Method for measuring liquid levels using the arrangement according to at least one of Claims 1 through 8 and 9 and/or 10, characterized in that jumps in the resistance values upon movement of a bubble are detected by parallel monitoring of the resistance values of all electrode pairs, and the path distance traveled by the bubble is determined from the number of jumps.

15. Method according to at least one of Claims 13 or 14, characterized in that the displaced liquid volume is determined from the path distance traveled.

16. Method according to at least one of Claims 11 through 15, characterized in that the resistance measurement of the electrode pairs is performed by measuring the resulting current after an alternating current is applied to the electrodes.

17. Method according to Claim 16, characterized in that the alternating current has a frequency in the kilohertz range and/or an amplitude in the range of 100 millivolts.

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Abstract

Disclosed is a sensor element for electrically measuring the position of liquid levels, comprising a substrate (2) and a plurality of electrodes (3) that can be contacted individually and that are mounted on the substrate, characterized in that the electrodes comprise sensor-active partial electrodes (5) that are networked with electrical connections (7), with the partial electrodes of two respective electrodes always being positioned opposite one another, separated by a distance, as partial electrode pairs (11), and with the electrode pairs (8) thus formed recurring periodically over the length of the sensor. Quasi-digital measuring methods are derived from the behavior of the impedance of the electrode pairs, whereby the liquid level is measured by detecting a conductivity boundary in a capillary filling.

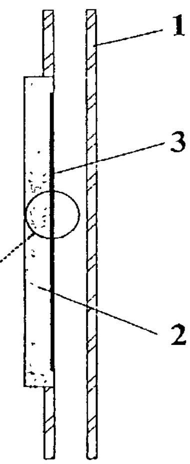

Fig. 1

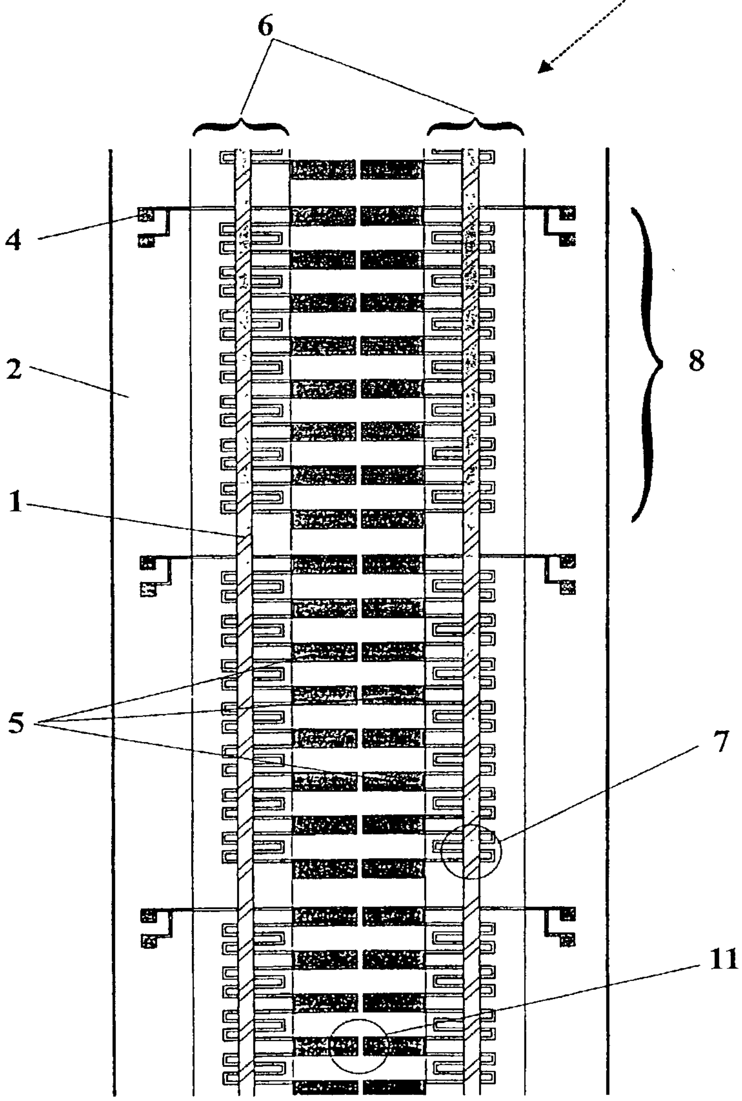

Fig. 2

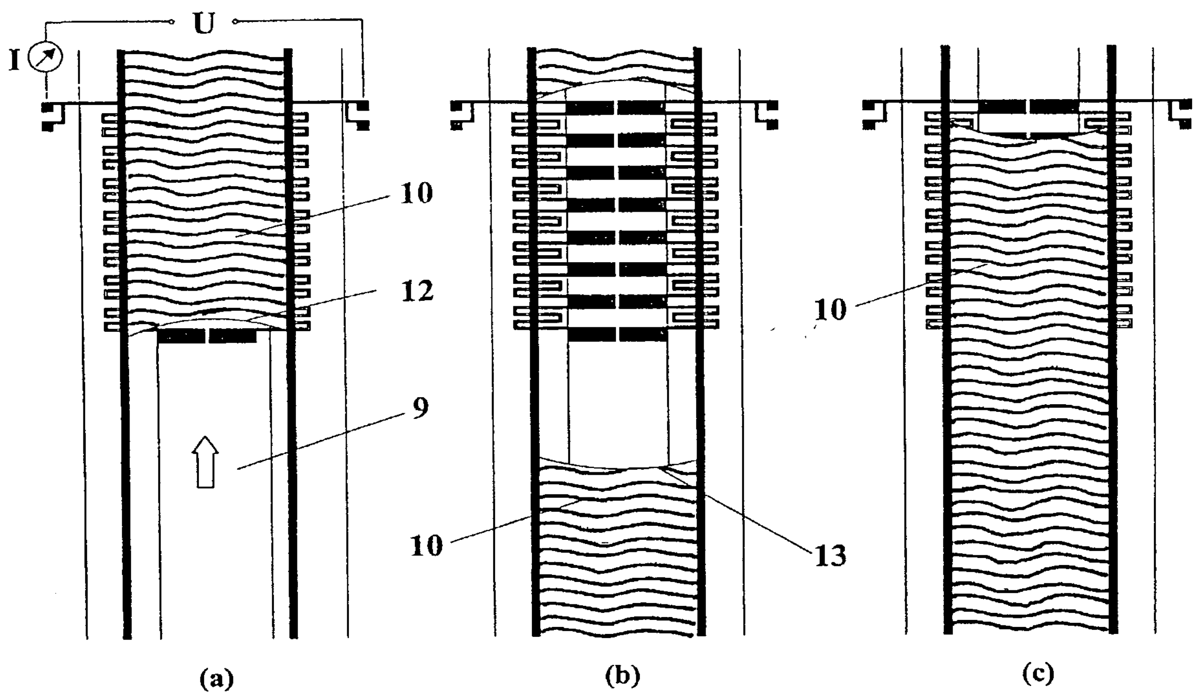

Fig. 3

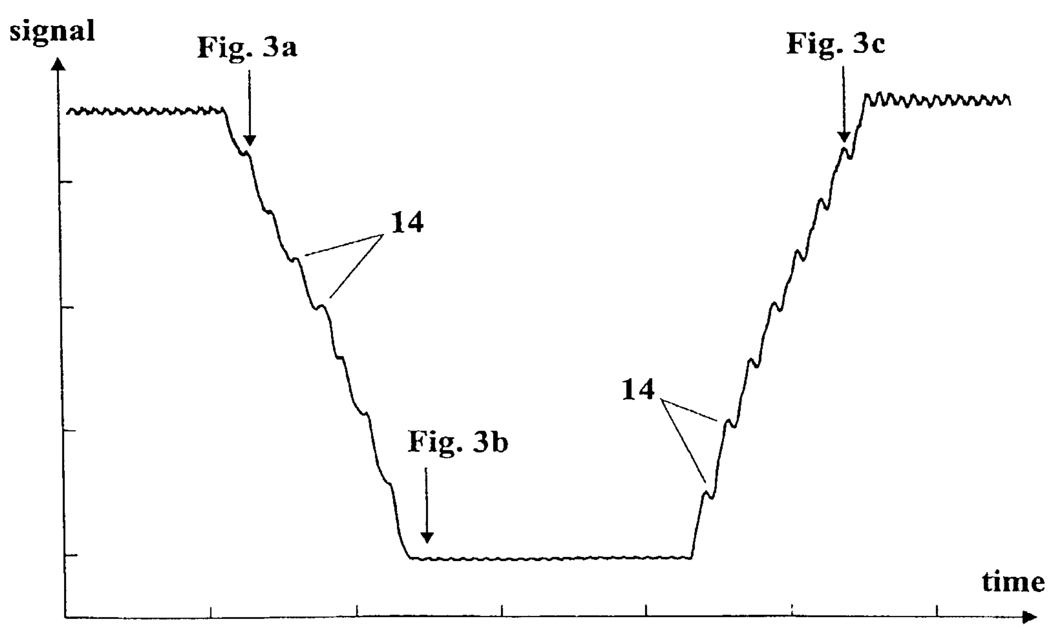

Fig. 4

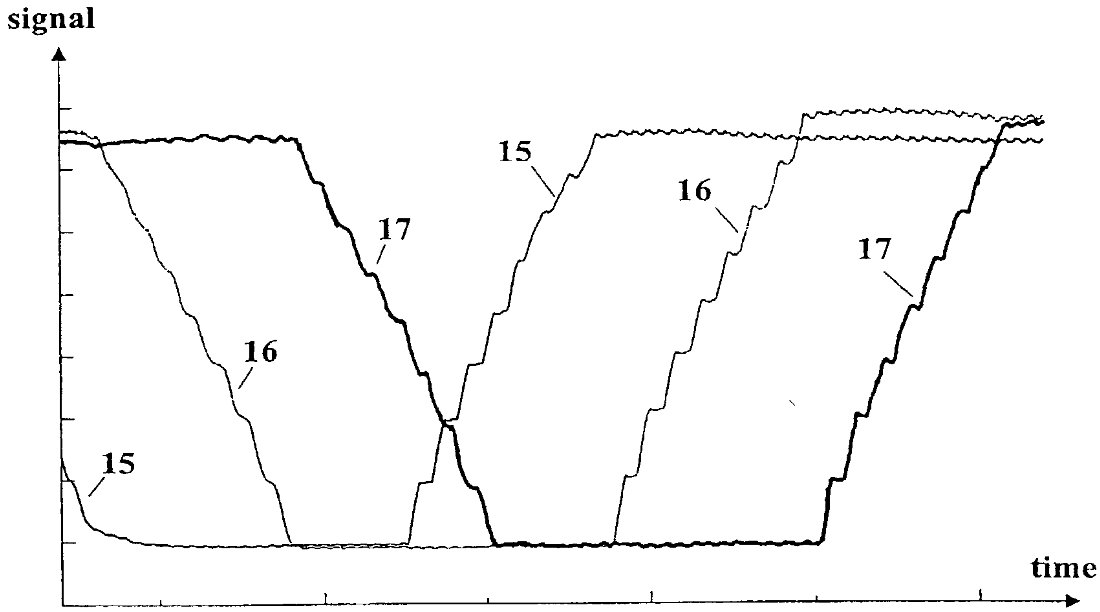

Fig. 5

COMBINED DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY (includes Reference to PCT International Applications)	ATTORNEY'S DOCKET NUMBER 127FR/50898

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

MICROSENSOR FOR MEASURING THE POSITION OF LIQUIDS IN CAPILLARIES

the specification of which (check only one item below):

[ ] is attached hereto.

[ ] was filed as United States application
Serial No.
on
And was amended
on _______________ (if applicable).

[X] was filed as PCT international application
Number PCT/DE00/02609
on 3 August 2000
and was amended under PCT Article 19
on _______________ (if applicable).

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to the examination of this application in accordance with Title 37, Code of Federal Regulations. §1.56(a).

I hereby claim foreign priority benefits under Title 35, United State Code, §119 of any foreign application(s) for patent or inventor's certificate or of any PCT international application(s) designating at least one country other than the United States of America listed below and have also identified below any foreign application(s) for patent or inventor's certificate or any PCT international application(s) designating at least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application(s) of which priority is claimed:

PRIOR FOREIGN/PCT APPLICATION(S) AND ANY PRIORITY CLAIMS UNDER 35 U.S.C. 119:

COUNTRY (if PCT indicate PCT)	APPLICATION NUMBER	DATE OF FILING (day, month, year)	PRIORITY CLAIMED UNDER 35 USC 119
Germany	199 44 331.9	15 September 1999	[XX] Yes [ ] No
			[ ] Yes [ ] No
			[ ] Yes [ ] No
			[ ] Yes [ ] No
			[ ] Yes [ ] No

10088200 .072202

Combined Declaration For Patent Application and Power of Attorney (Continued) (includes Reference to PCT International Applications	ATTORNEY'S DOCKET NUMBER 127FR/50898

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) or PCT international application(s) designating the United States of America that is/are listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in that/those prior application(s) in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, §1 56(a) which occurred between the filing date of the prior application(s) and the national of PCT international filing date of this application:

PRIOR U S. APPLICATIONS OR PCT INTERNATIONAL APPLICATIONS DESIGNATING THE U.S. FOR BENEFIT UNDER 35 U S.C. 120

U.S. APPLICATIONS			STATUS (*Check one*)		
U.S. APPLICATION NUMBER	U.S. FILING DATE		PATENTED	PENDING	ABANDONED
PCT APPLICATIONS DESIGNATING THE U S					
PCT APPLICATION NO	PCT FILING DATE	U.S. SERIAL NUMBERS ASSIGNED (IF ANY)			

POWER OF ATTORNEY: As a named inventor, I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith. (List name and registration number)

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I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true: and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon

SIGNATURE OF INVENTOR 201	SIGNATURE OF INVENTOR 202	SIGNATURE OF INVENTOR 203
Thomas Lisec	Bernd Wagner	H. J. Quenzer
DATE 13.03.02	Date 13 march 2002	DATE 3 march 2002